it allegedly contains HYAFF®, pore-forming agents, tricalcium phosphate, BMPs, and solubilizing agents\. The Examiner also contends that there is no indication that Valentini's solution intermediate is not injectable. Applicants respectfully disagree with this characterization of Valentini, and thus, with the Examiner's conclusion that the instant claims are obvious in view of Valentini.

Valentini does not render the application obvious for the following reasons. First, neither the compositions of Valentini, nor obvious modifications thereof, possess all of the limitations of the instant claims. Second, neither Valentini nor the knowledge of one skilled in the art provide the necessary suggestion or motivation to modify the teachings of Valentini to produce the claimed invention. Therefore, Valentini does not render claims 1-5, 7, and 11 obvious. *Manual of Patent Examining Procedure*, Section 2143.

In the attached Declaration, Dr. Hyun Kim identifies himself as an inventor on both the claimed invention and the Valentini patent. As a result, Dr. Kim has intimate knowledge of the teachings of the Valentini patent. In his declaration, Dr. Kim explains the differences between the compositions of the Valentini patent and the claimed application. These differences provide the basis for the arguments set forth below.

Valentini does not teach or suggest all the limitations of the claimed invention

The Valentini patent describes a solid scaffold carrier for implantation of BMPs. The synthesis of this solid (non-injectable) scaffold includes a step where the hyaluronic acid derivative is in a liquid form. This intermediate is a thick, slurry-like material (col. 8, line 32) that is not injectable (Kim Declaration, page 2, lines 17-23). As set forth in the declaration, the Valentini intermediate contains pore former at concentrations and sizes

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that are prohibitive to injection. Therefore, the liquid intermediate compositions of Valentini do not meet the limitations of the claims, which recite "a composition for injectable delivery." In addition, the Valentini intermediate composition contains pore formers at levels that are inflammatory, non-biocompatible, or superphysiological (Kim Declaration, page 3, lines 3-4). Therefore, the Valentini intermediate compositions fail to meet the "pharmaceutically acceptable" limitation of the claimed invention, as well.

Valentini does not suggest modification

Valentini also fails to provide any suggestion to modify its compositions to render them "injectable." The Examiner, however, contends that there is no indication that the composition of the Valentini patent is not injectable. In fact, it is not injectable. Furthermore, this is insufficient support for a finding of obviousness. Rather, the Examiner must demonstrate that Valentini provides a motivation or suggestion of the desirability of modifying its teachings to arrive at the claimed invention. *Manual of Patent Examining Procedure*, Section 2143.01. The Examiner seems to believe that because Valentini does not explicitly teach away from injectable compositions, the suggestion to modify is implicit. This is an improper application of the law. The Federal Circuit has made its position on this issue clear in a number of cases, including In re Gordon: "The fact that the prior art device could be modified so as to produce the claimed device is not a basis for an obviousness rejection unless the prior art suggested the desirability of such a modification." *See, e.g., In re Gordon,* 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984). The mere absence of a "teaching away" does not satisfy

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this requirement. Therefore, Valentini does not provide the necessary suggestion for modification of the disclosed compositions to achieve an injectable composition.

In addition, Valentini does not contemplate the addition of BMPs to the intermediate composition. In Valentini's disclosure, BMPs are added to the final scaffold. The mere fact that a reference could be modified does not render the modification obvious; there must also be a suggestion or motivation in the reference to make the modification. *In re Mills,* 916 F.2d 680, 16 USPQ 1430 (Fed. Cir. 1990). Valentini does not even suggest the mixing of BMPs with its non-injectable liquid intermediate, let alone the combination of BMPs with any injectable composition, such as the ones described and claimed by Applicants. Therefore, it is only with the teachings of Applicants' specification that one skilled in the art is provided with the motivation to make a hyaluronic acid ester injectable vehicle for the delivery of osteogenic proteins.

In light of the above arguments and the attached Declaration, it is clear that Valentini does not teach, contemplate, or even suggest injectable compositions comprising hyaluronic acid esters and osteogenic proteins. The Valentini intermediate, considered by the Examiner to be equivalent to Applicants' invention, is not injectable, not pharmaceutically acceptable, and does not comprise osteogenic proteins. There are no teachings in Valentini that would lead one skilled in the art to the injectable, pharmaceutically acceptable composition of Applicants' invention.

Claim 6 is rejected under 35 U.S.C. § 103 as obvious over Valentini in view of U.S. Patent No. 6,187,742 (Wozney *et al*). The Examiner alleges that Wozney

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describes formulations of BMPs in carriers like porous particulate polymers, hyaluronic acid, and TCP. The Examiner then contends that the carriers of Wozney "are functionally equivalent and nearly the same as those of Valentini." (Office Action at page 3.) The Examiner concludes that it would involve nothing more than an arbitrary matter of experimental design choice to select one carrier over another. Applicants respectfully traverse this rejection.

In this situation, once again, the Valentini patent teaches away from the instant invention. Applicants point out that Valentini defines the hyaluronic acid of Wozney and the hyaluronic acid derivatives of the instant invention as possessing completely different characteristics, including differences in porosity and solubility (Valentini, col. 4, line 63-col. 5, line 47). Furthermore, claim 6 is dependent from claim 1 and thus patentable over Valentini for all the reasons set forth above. The combination of Wozney with the insufficient disclosure of Valentini does not cure the deficiencies of Valentini.

As set forth above, Valentini fails to suggest the combination of any BMPs with any injectable compound. In fact, Valentini teaches away from the use of its compositions as injectable carriers of BMPs. Wozney does not describe hyaluronic acid derivatives and provides no motivation for one skilled in the art to use the hyaluronic acid ester compositions of the claimed invention instead of the disclosed hyaluronic acid. Therefore, the combination of Wozney and Valentini is inappropriate, and in addition, fails to teach every limitation of the claims.

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Applicants submit that the claims recite an unobvious injectable vehicle for delivery of osteogenic proteins. Neither Valentini or Wozney, separately or together, support a *prima facie* case of obviousness. Therefore, Applicants respectfully request that the rejections of claims 1-7 and 11 under 35 U.S.C. § 103 be withdrawn.

In view of the foregoing amendments and remarks, Applicants respectfully request the reconsideration and reexamination of this application and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

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